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Knuckle pads: an ancient disease frequently misdiagnosed because of minimal modern attention

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Abstract

Knuckle pads are benign painless papules and nodules that most commonly appear on the extensor surfaces of the proximal interphalangeal joints. Knuckle pads are frequently misdiagnosed due to their location overlying joints, which can lead to costly interventions and patient discomfort for a relatively harmless condition. We describe a 44-year-old woman who presented with mildly painful nodules on multiple bilateral proximal interphalangeal joints. The patient did not have a family history of fibromatosis and the rheumatoid factor was negative. Histology showed mild epidermal hyperkeratosis, papillomatosis, and acanthosis with a deep dermal, poorly circumscribed, proliferative nodule made of spindled myofibroblasts without cytological atypia. The diagnosis of knuckle pads was established based on the clinical and morphological presentation of the nodules. Treatment with intralesional triamcinolone acetonide injection produced significant clinical improvement. Our findings highlight the challenging diagnosis of knuckle pads and the importance of increasing the familiarity of knuckle pads in modern medical practice.

Keywords: fibromatosis, heloderma, knuckle pads, proximal interphalangeal joints

Introduction

Knuckle pads (KPs), also known as Garrod pads or heloderma, were initially described by Garrod over

120 years ago but have been recognized for centuries [1]. Michelangelo's statues of David in Florence and Sleeping Slave in Paris highlight the presentation of knuckle pads on the hands [2]. Unfortunately, in modern times, knuckle pads have received minimal attention in the medical literature, resulting in unnecessary diagnostic challenges.

Case Synopsis

A 44-year-old woman accountant was referred to the dermatologist by her rheumatologist for joint pain and nodules on the knuckles. The patient reported gradually worsening joint pain in her fingers over the last several years which was exacerbated by typing. Over the last two years, she began noticing swelling over her interphalangeal joints. The patient was also concerned with the aesthetic appearance of the



Figure 1. Knuckle pads over the proximal interphalangeal joints of the right 2nd, 4th, and 5th and left 2nd to 4th fingers.

lesions. Rheumatoid factor was normal (negative). X-rays of the hands failed to identify bony or soft tissue changes of an arthropathy. Family history was unremarkable, without similar cases. The skin examination demonstrated firm, slightly mobile subcutaneous nodules of multiple bilateral proximal interphalangeal joints (**Figure 1**). The skin overlying the nodules appeared atrophic and shiny. The clinical differential diagnosis included rheumatoid nodules, gout, calcinosis cutis, and subcutaneous granuloma annulare. Histopathology demonstrated mild hyperkeratosis, papillomatosis, and acanthosis (**Figure 2A, B**). In the deep dermis and subcutis, there was a poorly circumscribed cellular proliferation of epithelioid and spindle-shaped myofibroblasts (**Figure 2A, C**). There was no evidence of cytological atypia and mitoses were not detected. Randomly oriented scattered blood vessels were present within the nodule (**Figure 2C**). Based on the clinical and histopathologic features, the diagnosis of knuckle pads was established. The patient was thereafter treated with intralesional triamcinolone acetonide injection (10 mg/mL in 0.1-0.2 mL aliquots per lesion). Clinical improvement and patient satisfaction were achieved after only one injection, with plans to repeat if patient desires in the future (**Figure 3**).

Case Discussion

The relative unfamiliarity with KPs among general practitioners, dermatologists, and rheumatologists may lead to extensive, high-priced evaluations for a

harmless disorder. Knuckle pads can occur at any age but are more common between 15 and 30 years of age [3]. Knuckle pads present as painless nodules that are more commonly seen as multiple papules over the extensor surfaces of finger joints but can also be solitary. Typical lesions are slightly pink or skin-colored but may be hyper- or hypopigmented in darker skin types [3,4]. The overlying skin may appear normal, wrinkled, or atrophic.

Knuckle pads may be primary or secondary (acquired). Most primary cases are idiopathic in origin and demonstrate an equal sex incidence [2,3,5]. Primary KPs are more common in patients with other forms of fibromatosis such as Dupuytren contractures, Ledderhose disease, or Peyronie disease [6-10]. Primary KPs may also represent a syndromic manifestation of Bart-Pumphrey syndrome, acrokeratoelastoidosis of Costa, Vohwinkel syndrome (palmoplantar keratoderma), camptodactyly, keratoderma hereditary mutilans, or pseudoxanthoma elasticum [11-14]. Some primary causes can also result from *KRT9* mutations [15-18]. Primary knuckle pads represent a form of fibromatosis, which is reflected by the characteristic histopathological features.

Primary KPs should be distinguished from secondary (acquired) or pseudo-knuckle pads, which result from distinct pathophysiology. Secondary KPs are induced by repetitive trauma and represent a form of callus over the interphalangeal joints [19-20]. They are common in boxers, carpet layers, and other professions with repetitive knuckle injury [3,21].

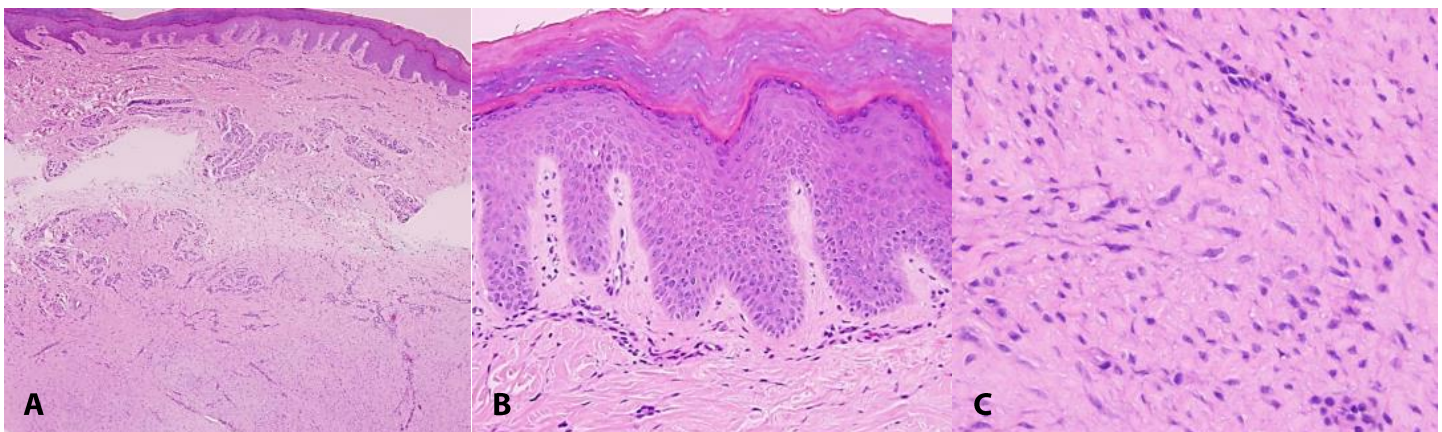


Figure 2. H&E histopathology: **A)** punch biopsy of acral skin with dermal/subcutaneous spindle cell proliferation, 20x; **B)** epidermal papillomatosis and acanthosis, 200x; **C)** proliferation of epithelioid and spindle-shaped myofibroblasts in the deep dermis, 200x.

Secondary KPs may also be observed in athletes, surfers, and runners [22,23]. In addition, secondary KPs are also commonly seen in patients with obsessive-compulsive disorder and bulimia [24]. Secondary KPs demonstrate pronounced hyperkeratosis, hypergranulosis, and acanthosis with similar histopathological features observed in callus [2]. Unlike primary KPs, fibrosis is mild and limited to the superficial dermis.

As a result of their location overlying joints, patients with KPs are frequently referred to rheumatologists to exclude rheumatoid nodules, gouty tophi, Heberden nodes, or synovitis [25,26]. Patients with KPs are also referred to dermatologists, for whom the differential diagnosis may include granuloma annulare (GA), erythema elevatum diutinum (EED), pachydermodactyly, or even verruca [13,27-32]. Granuloma annulare has an annular appearance not observed in knuckle pads and can be present on other parts of the hand [27]. Granuloma annulare

demonstrates interstitial or palisaded necrobiotic granulomas with mucin [28]. Erythema elevatum diutinum presents with red or brown papules and plaques, is not limited to the skin overlying joints, and is characterized by leukocytoclastic vasculitis with prominent fibrosis [29]. Pachydermodactyly is very rare and characterized by fusiform swelling involving the entire interphalangeal joints [13]. In contrast, knuckle pads are limited to the extensor surface of joints. Verrucae vulgares are papillomatous, small, skin-colored papules that are not limited to the skin on hand joints [30].

Recognizing KPs based on clinical presentation is important to avoid expensive workups and provide reassurance to patients. It is also important to separate primary from secondary or pseudo-knuckle pads. Treatment of primary KPs can be difficult, although injection of intralesional triamcinolone cause improvement. Secondary KPs can resolve within months if a cause of trauma is identified and removed [31].

Conclusion

Knuckle pads can be divided into primary (idiopathic) and secondary (acquired) subtypes. Treatment options for the two subtypes are vastly different, with primary or familial knuckle pads proving more difficult to treat, whereas secondary knuckle pads can be more easily resolved if the source of trauma is identified. Diagnosis is based on the clinical presentation of the nodules and differentiation between subtypes is necessary to avoid expensive workups and decide the proper course of treatment and management. Our findings highlight the challenging diagnosis of knuckle pads and the importance of increasing the familiarity of knuckle pads in modern medical practice.

Potential conflicts of interest

The authors declare no conflicts of interest.

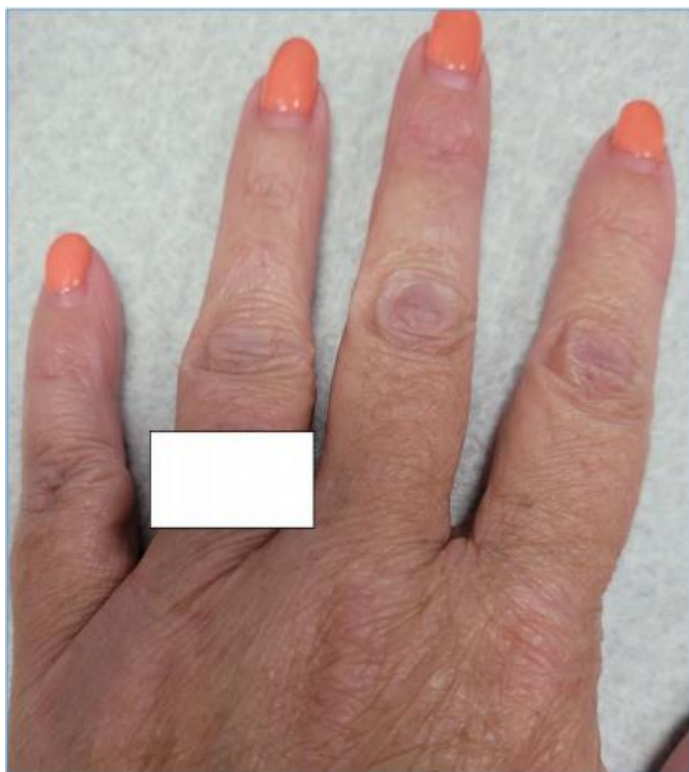


Figure 3. Knuckle pads four weeks after treatment with intralesional triamcinolone acetonide injection.

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